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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

JOHN F. McCLOSKEY
1894-1957
The late Dean of the College of
Pharmacy, Loyola University
Educator, Historian, Philosopher and Friend

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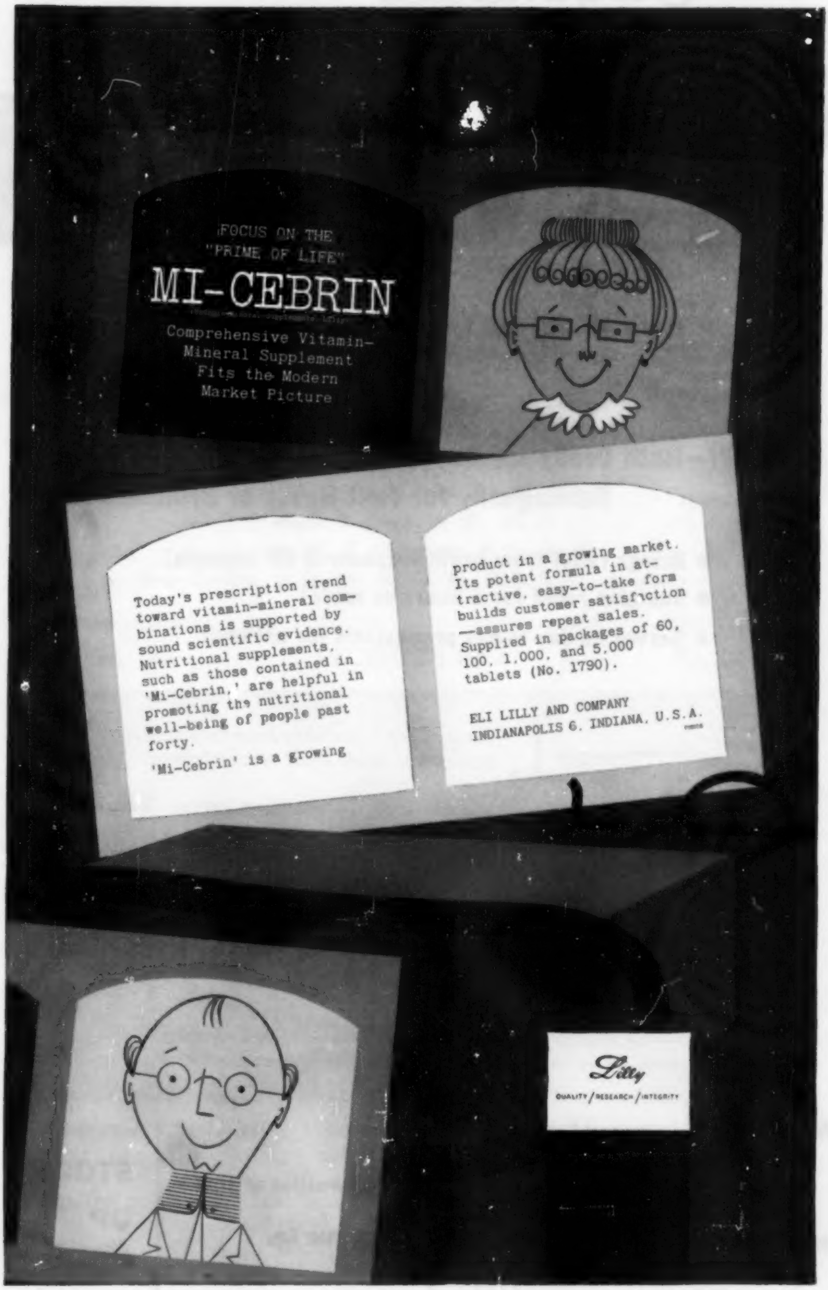

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AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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E D I T O R I A L

"SPUTNIK'S" SIGNIFICANCE

SO much has been said and written about the Russian earth satellite that one hesitates to add still further comment to its significance. In reading of the reaction of our political leaders and most other people, the true meaning of this achievement seems almost to be lost.

In the first place, one should not minimize the significance and technical accomplishment which placing these satellites in orbit represents and those who are imbued with the true spirit of science must pay their respects to those in Russia who are responsible for this scientific masterpiece. From the scientific standpoint, it undoubtedly ranks with the top ten advances of science in man's history. The early attempts on the part of some Americans to shrug it off and to say that we could have done it a year ago had we wished is unsporting in the first place and pure buncombe as well.

Now that we have given credit to the Russians for what they have done, it is of importance to stop for a moment and consider not just why they got to do this before us but whether our failure in this respect may be an early sign of a deep, underlying malady which is beginning to afflict our nation and our society. There are many other symptoms of the same thing but few people make any effort to connect them. There are, moreover, case histories available of other great nations which were once strong and hardy but in which this same disease process finally took its toll and ended in death. The really important question is whether Americans recognize this lingering illness and take the heroic measures required to stem the disease. With the present complexion of thought in the United States, this does not seem too promising or likely.

We in the United States are suffering today from many evils all stemming from the firm belief that Americans are the greatest people in the world—, the smartest, the strongest, the most versatile, the most resourceful, and those in whom God has placed his trust to save humanity. What is even worse, we believe we are so good that no-one needs to study, think, or work hard to carry out our destiny. We

just can't fail! This all begins in the home with the young child who is taught from the very beginning to expect something and, indeed, almost everything for nothing. Discipline of both mind and body are looked upon as old-fashioned ways of bringing up children. They must be permitted to express their individuality. When they finally reach school age, this system is extended since teachers are under great pressure not to undo the poor job that has already been done. Consequently, very few children really are required to apply themselves diligently while gaining an education. The courses which now are widely taught American youth teach them to be better citizens—whatever this means—and all courses which discipline and strengthen the intellect, particularly those studies in the physical sciences are shunned. No real effort is made to obtain teachers who believe in high standards and who can really teach these difficult courses. We, the richest nation in the world, cannot afford to pay our teachers as much as a truck driver makes. The process does not stop here since it permeates the entire field of higher education.

Even more significant is that recent studies have shown that high school students and probably their parents as well have a very low regard for scientists including college teachers, and very few indeed wish to emulate them. The scientist is still looked upon by the general public as sort of a harmless fellow somewhat amusing and usually pitied. The public looks upon him with a sort of kindly indulgence but not at all to be compared with their great heroes in the field of baseball, the movies, and others in the entertainment world. The successful man to them is the man with money. It does not matter too much what else he has or lacks.

When we contrast this, our system, with that in Russia, it is no wonder that they are rapidly overtaking us in the field of science. Their scientists and teachers are looked upon with profound respect as the true architects of the future which, indeed, they are. Even small children are taught to look up to them and every student works to the best of his ability hoping someday to reach that pre-eminence on which some scientist, his hero, stands. Even the government gives its full support to this process and college professors are among the highest paid vocations in Russia with all sorts of other benefits given them by reason of their station in the scheme of things.

"But", some readers will say, "We have our freedom". "We can do as we like". "No system which regiments the individual can possibly match ours". This may be true and let us hope that it is.

But some few Americans who are giving this matter thought wonder whether in the final analysis our system will prove superior. It undoubtedly would if we could depend upon our people to use their freedom with dedication to purpose, hard work, and self-sacrifice. If, on the other hand, we use it in the typical American way of providing for ourselves a life of ease and luxury, avoiding all things which are difficult and unpleasant, the American experiment may fail. In Russia, all effort is concentrated on the achievement of those goals essential to their global supremacy and not in an attempt to outdo all other nations in conspicuous consumption.

The ancient Greeks of Athens were highly civilized and possibly far superior to their neighbors but this did not save them from being overwhelmed by people who had other values and a hardier existence.

Americans in all walks of life would do well to give more thought to where we are going and how we propose to get there. At the moment, most of us seem to be squeezing out of life and our nation that which we can get and enjoy without much thought of tomorrow.

As a final thought, it might be well for us to pause for a moment in our headlong race with Russia for arms and technological supremacy and consider our moral and spiritual values. Is it not possible that our ultimate survival as well as that of the rest of the world depends more on these than on arms alone? While we must be strong, is it enough to be prepared to meet force with force? Does it help to hurl insult for insult and refuse to make any concession or compromise. This has never brought peace in the past and it is not likely to achieve results now. Has the time not come to give the admonition "Love thine enemies" some little place in international relations or have we gone so far astray that we no longer believe in the philosophy and teachings of Christ?

L. F. Tice

STERILIZATION OF FLUIDS BY MEANS OF STEAM UNDER PRESSURE *

By T. B. Owen **

IT is the purpose of this paper to present briefly the application of steam under pressure as an agent for sterilizing flasked fluids. Most of the discussion will be directed toward sterilization of large volume products, i.e., quantities of 500 or 1000 milliliters. The principles, however, are certainly applicable to smaller volume containers. I am sure that pressure steam equipment which is available to most of this group is of standard design for hospitals. Therefore, my remarks are directed toward conditions in which an adequate supply of saturated steam under pressure is available for use in hospital sterilizers with standard piping, venting, and controls.

The modern bulk sterilizer for the hospital is a jacketed machine, and steam is emitted to the chamber from the jacket at some point in the upper rear portion of the chamber. (Figure 1.) This process continues until all air is voided from the chamber through the chamber drain line, and the desired exposure temperature is attained in the chamber. The sterilizing temperature usually employed is 250° F. or 121° C. which is the temperature of saturated steam under 15 psig. at sea level. It might be well to note that the steam pressure gauge in hospital probably will be adjusted to 17 or 18 lbs. pressure; these adjustments being made to compensate for variations in atmospheric pressure at different altitudes.

The temperature of 250° F. is maintained by means of a thermostatic trap. This trap is a vital part of the sterilizer. Its primary function is to allow air and condensate to escape to the waste line, thereby maintaining proper sterilizing conditions during the entire exposure period.

Pressure alone is not indicative of proper sterilizing conditions, and even though the terms pressure and time are still used on occasion, they leave much to be desired in describing the physical conditions

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** Research Associate, American Sterilizer Company, Erie, Pennsylvania.

necessary for sterilization. The fact that sterilizing conditions are solely dependent upon the inter-relationship of time and temperature cannot be overemphasized. It is possible, experimentally, to trap air inside the chamber and obtain a pressure of 15 psig. but the temperature may reach only 230° F. The screen plug in the front bottom of the chamber has been placed there specifically to avoid this hazard. (Figure 2.) This screen should be checked daily and kept free of lint, caramelized dextrose, and corrosion from sodium chloride or other agents.

For our purposes today, we may say that all solution loads should be processed utilizing a "Slow Exhaust." We will have more to say concerning the physical conditions inside the chamber during the exhaust period, but for the present we will consider only the control provided for exhausting solutions. (Figure 3.) Most hospital

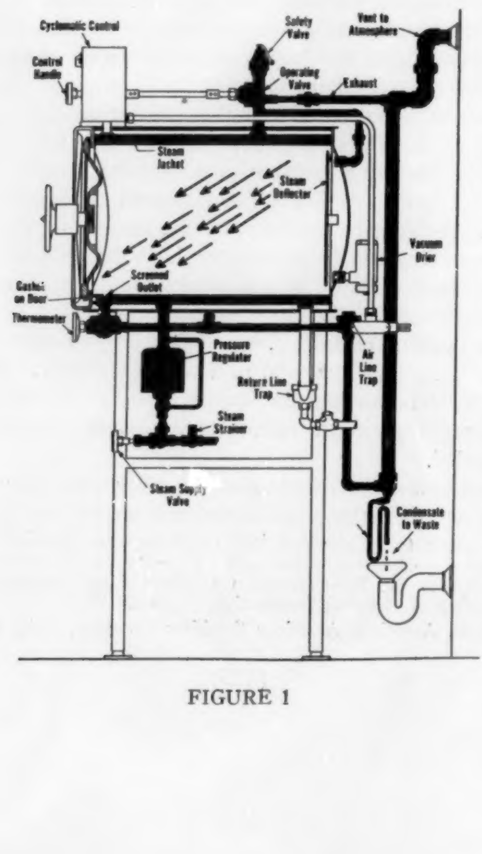

FIGURE 1

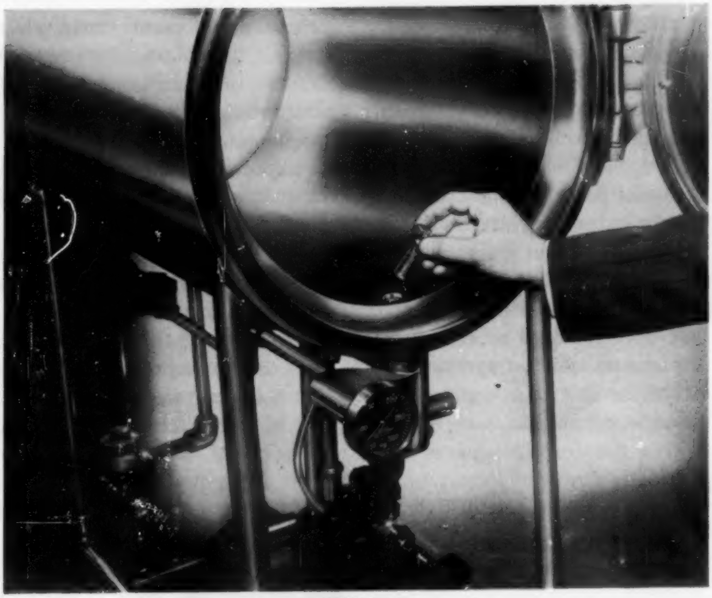

FIGURE 2

FIGURE 3

sterilizers are supplied with a control whereby the operator may select either a "Fast Exhaust" or a "Slow Exhaust". In situations in which a manually controlled unit is available, this selection is made at the end of the exposure period by turning the handle or knob to the "Slow Exhaust" position. In the case of the automatic type of control which is illustrated in Figure 3, the desired exposure period and exhaust are selected before the cycle is started, and the necessary timing and proper exhausting are carried out according to the settings.

In any given glass container of aqueous fluid being sterilized by steam under pressure, a certain period of time is required to raise the temperature of the contents of the container to the desired temperature. We may consider a theoretical column of fluid at the center of the container as the last portion to come up to desired temperature. (Figure 4.) This is not a stationary column under practical conditions because convection currents instigated by temperature differentials within the container cause some circulation of the fluid. Experimentally, however, it may be shown that the center area of the container shows the greatest lag. This area, then, becomes the most critical from the standpoint of proper exposure.

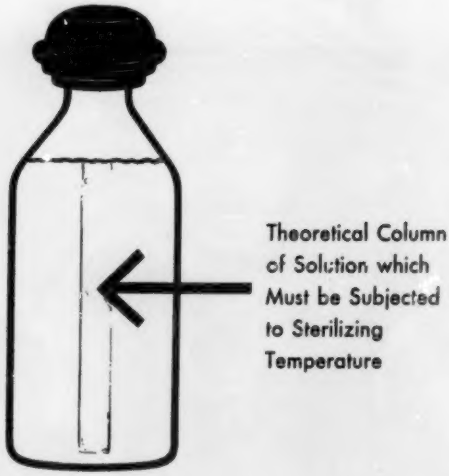

FIGURE 4

When steam is admitted to the chamber, it contacts all points on the outer surface of the container, and pressure is exerted from the outside toward the inside. (Figure 5.) It should be noted that steam will contact the inner part of the container during this period unless the container has a "one-way valve" or is sealed hermetically.

The method of heat transfer to the inside of a glass container is entirely different from heat transfer to the inside of a muslin wrapped pack. We are familiar with the process of steam penetration of packs with subsequent condensation and liberation of heat to the material. Heat transfer to the center of a flask is dependent upon additional factors; namely, convection, conduction, and radiation. (Figure 6.) The two most important factors to be considered here are convection and conduction. The temperature of the outer wall of the container is raised when steam strikes the surface and condenses. The heat is then transferred through the glass and to the fluid by conduction.

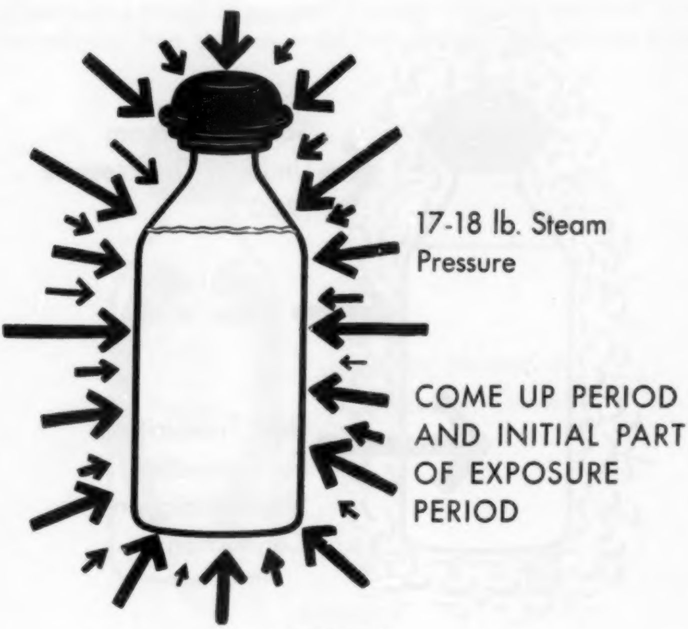

FIGURE 5

The temperature of the fluid nearest the glass is raised and this fluid rises toward the top of the container. (Figure 7.) For practical purposes we may visualize these convection currents as rising around the inner sides of the container and converging at the top center of the liquid, then down the center to the bottom.

The transfer of heat by convection, along with some conduction, eventually brings the entire contents of the container to the temperature and pressure of the surrounding steam. (Figure 8.) It is readily seen that the chamber drain line thermometer may reach the desired temperature in a relatively short period of time, but additional time is required to bring the entire contents of the containers to the same temperature. This lag will vary with the type and size of containers and to some extent with the type of fluid therein. It is evident that many things should be considered in determining the correct exposure period for a given package. In most cases, this information can be obtained from the manufacturer of the *container* being used.

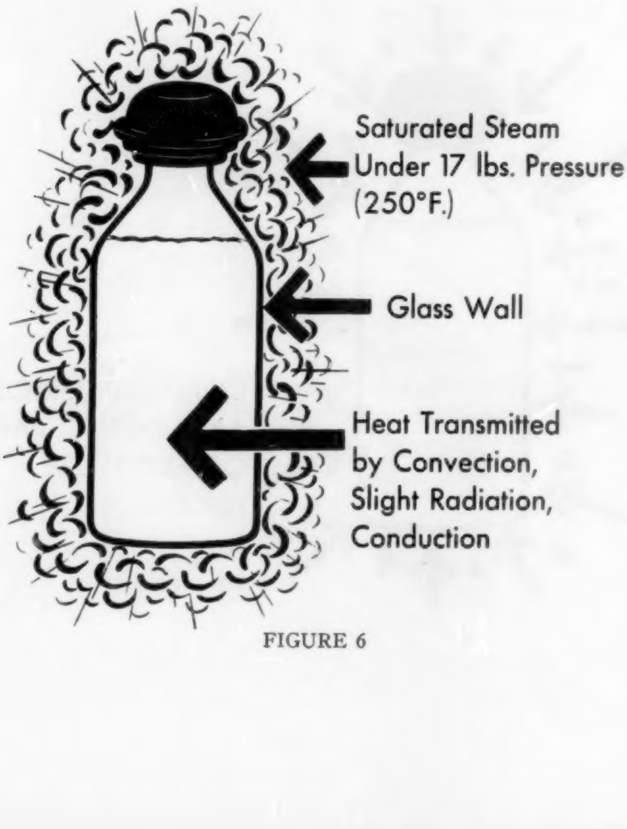

FIGURE 6

Following the correct exposure period, steam is exhausted from the chamber either automatically or manually, depending upon the type of sterilizer control. The transfer of heat within the container during this period is practically the same as during the initial heating period but the direction, of course, is reversed. The critical factor from the practical standpoint during the exhaust period is pressure. (Figure 9.) The pressure exerted within the container has a direct relationship to the temperature of the aqueous fluid being sterilized. The differential in pressure created between the inside of the container and the inside of the chamber during the exhaust period is of vital importance.

It was mentioned previously that two general types of closures are available to the hospital today. Either of these types may be used successfully provided the proper precautions are taken. The "venting" type of closure provides a safeguard by allowing steam to escape from the inside of the flask with subsequent cooling of the contents. Generally speaking, this type of closure will vent when an excess of one to two pounds of pressure is created within the container. The loss of water from the fluid in the form of steam is considered in the

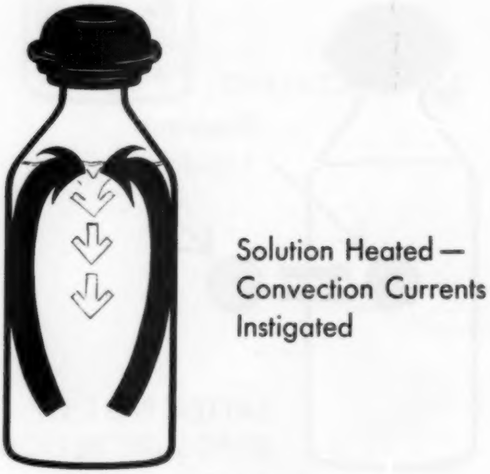

FIGURE 7

initial preparation of the fluid. Even though this loss will vary with container size, the factor is constant. Compensation, therefore, is made for this loss before the fluid is subjected to sterilization.

The second type of closure in general use in hospitals permits the flask to be sealed hermetically before sterilization. Since there is no provision for venting, the build-up of pressure within the container during the exhaust period is even more critical. Should this pressure exceed the stress tolerance of the container, some portion will crack. When closures of this type are employed, extreme care should be taken in regard to the exhaust procedure, as well as during removal of the load from the sterilizer. Unfortunate accidents have occurred in some cases wherein excessive pressure within the flasks caused explosions when the load was removed from the sterilizer.

There are many factors to be considered in regard to sterilizing fluids in any given container.

It is the pharmacists' responsibility to see that proper principles and methods of sterilization are applied at all times. Due regard should be given safety factors in relation to obtaining sterility of a product and in relation to the welfare of attending personnel. Infor-

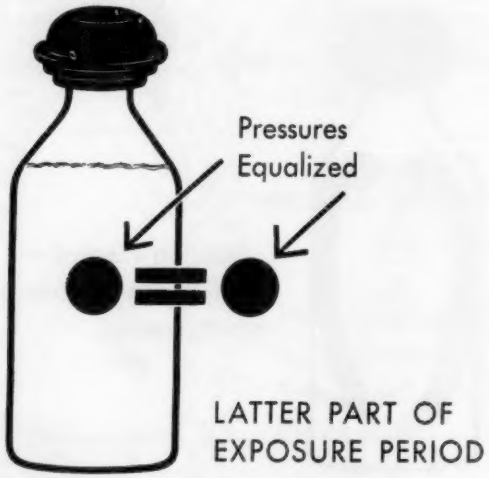

FIGURE 8

mation in regard to correct exposure periods for containers usually may be obtained from the manufacturer or other reliable sources. If such information is not available, it then becomes the pharmacists' responsibility to determine the necessary conditions for obtaining sterility of the product prior to dispensing.

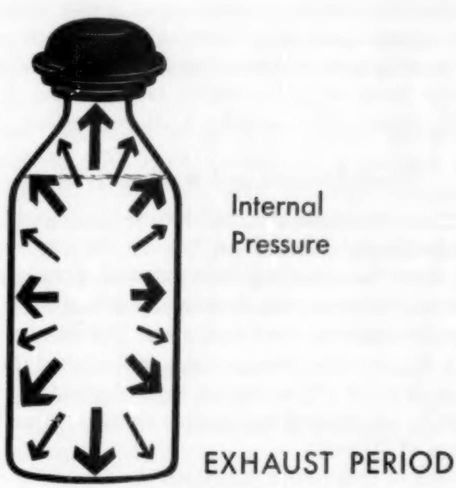

FIGURE 9

INORGANIC CARCINOGENS

By C. Stuart Patterson and John R. Sampey *

A recent study by the authors on the treatment of cancer with inorganic chemicals (200) cited 129 references to the current medical literature. The present paper reviews 200 investigations on the carcinogenic action of inorganic agents. More than one-half of these reports deal with the cancer inducing or cancer promoting action of radioactive isotopes and other inorganic radiations. Among the non-radioactive inorganic chemicals the largest number of investigations have been made with compounds of chromium [23 reports], beryllium [18], arsenic [13], asbestos [12], and silicon [8].

Radioisotopes and Radioactivity

Radioiodine. Administration of I^{131} induced neoplasms in the thyroid of experimental animals (47, 74, 75, 76, 78, 79, 128, 137). Maloof (135, 136), however, reported only one adenoma in 500 rats subjected to 1 to 300 microcuries of radioiodine, and Field, et al. (61), noted no neoplastic changes in rats given 273 mc. of the isotope. Dailey, et al. (38), and Freedberg, et al. (66), studied the histological effects of small doses of I^{131} on human thyroid glands. Taylor (181) was unwilling to recommend radioiodine therapy to patients with a life expectation of 20 years.

Large doses of radioiodine destroyed the thyroid in experimental animals, and produced pituitary neoplasms (27, 28, 44, 56, 57, 68, 69, 70, 71, 77, 83, 84, 85, 92, 171). Gorbman (80, 81, 82) produced tumors of the pituitary and trachea in mice with massive doses of radioiodine, and Silberberg (172) noted joint lesions in mice thyroidectomized with the isotope. King, et al. (119), described carcinoma of the larynx in a patient receiving I^{131} therapy.

Several cases of acute leukemia have been reported in patients receiving radioiodine. Blom, et al. (12), described a case after receiving 3900 r in 1948 for carcinoma of the thyroid, and 261 mc. of I^{131} in 1951-52 which ended fatally in 1952 in acute leukemia. Delarue, et al., observed a similar case in a patient receiving 324

* Furman University, Greenville, South Carolina.

mc. of the isotope, and Seidlin, et al. (166, 167, 168), recorded several cases of acute myeloid leukemia following prolonged use of radioiodine.

Radiophosphorus. Brues, et al. (24), found P^{32} was comparable to x-rays as a carcinogenic agent in mice. Moore, et al. (150, 151), caused squamous-cell carcinoma in the forestomach of mice by intragastric balloons filled with the isotope. Moller (146) and Koletsky (121, 122, 123, 124) induced osteogenic tumors in rodents with injections of radiophosphorus. This agent also enhanced the growth of several transplanted cancers in experimental animals (15, 18, 19, 20).

Radiogold. Botsford, et al. (17), noted hypoplasia of bone marrow associated with Au^{198} therapy in 6 patients with various cancers. Williams, et al. (190, 191), reported that the isotope increased liver damage in rats fed the carcinogen, 3′-methyl-4-dimethylaminoazobenzene, while several investigators described liver tumors in laboratory animals, following radiogold administration (91, 96, 123, 184, 186). Bollag (15) promoted the growth of mouse Crocker sarcoma transplants with injections of the isotope.

Uranium. Uranium induced bone cancer in rodents (62, 103), and sarcoma in the chest walls of rats (103). The high incidence of lung cancer in many miners of uranium in Germany and Bohemia has been known for years (176).

Plutonium. Bone tumors have been produced in rodents by Pu^{239} (62, 130).

Astatine. At^{211} or eka-iodine, caused more destruction of the thyroid glands in rats and monkeys than did radioiodine (93), and a high incidence of breast tumors were observed in rats, following doses of At^{211} (94).

Radiocerium. Lung tumors developed in rats breathing Ce^{144} in the form of its oxide, CeO_2 (129).

Radiostrontium. Bone tumors were found in mice after a single injection of Sr^{89} (63), while muskrat feeding on plants containing Sr^{90} developed bone sarcoma, too (125).

Radiosodium. Hypophyseal tumors appeared in mice exposed to Na^{24} after thyroidectomy (56, 57).

Radiocobalt. Burkell, et al. (26), described less skin reaction to Co^{60} than that observed by x-rays.

Other Radioactive Material

Thorotrast. A number of human cancers have been traced to the use of thorotrast as a contrast medium, including liver tumors (67, 98, 132, 143, 164, 198), spindle-cell sarcoma of the pelvis (114), sinus epithelioma (88), epithelium carcinoma (163), lung carcinoma (1), and breast cancer (25). Hueper (101) included ThO_2 in his study of the role of environmental agents in the causation of human neoplasms. Injections of thorotrast in experimental animals resulted in malignant tumors (90, 115, 197).

Radioactivity. A mortality of 50% from lung cancer in workers in the radium mines of Jackymov, Bohemia, focused attention on the perils of atmospheric irradiations (170). A number of current studies are being conducted on radiation hazards from atmospheric and environmental sources (2, 13, 36, 37, 40, 106, 107, 116, 117, 134, 157, 160, 179). The incidence of leukemia and other neoplastic diseases among survivors of atomic bombings in Japan are also an active field of investigation (35, 64, 72, 126, 147, 148, 149, 177, 196). The high incidence of cancer among radiologists and x-ray technicians has also received attention (60, 141). Van Allen (187) has warned of the use of fluoroscopes in shoe-fitting. Cancer has resulted in laboratory animals following ionizing irradiation (185) and radon seeds (144).

Non-Radioactive Inorganic Chemicals

Chromium. The high incidence of lung cancer among workers in chromate plants has been well established (5, 6, 9, 10, 13, 23, 86, 87, 107, 111, 133, 138, 139, 140, 179). Further studies of occupational cancer from chromates include (21, 101, 105, 157, 183, 194). Hueper (109) produced bone and lung carcinomas in rats by parenterally introduced metallic chromium and chromate ore.

Beryllium. Studies have been conducted on acute dermatitis among Be workers (42, 43), while Eisenbud, et al. (58), reported 11 persons who lived near a Be plant, but were not employees, showed chronic beryeliosis. Two reports of beryllium granulomas of the skin have been filed following the accidental breaking of fluorescent lamp

tubes which were lined with Be compounds (52, 127). Neoplasms have been induced in laboratory animals by administration of beryllium oxide (39, 53, 54, 55, 99, 153), and beryllium silicates (7, 8, 34, 113, 153, 174, 175). Suspensions of Be in lanolin caused neoplasms in rats (108).

Arsenic. Several human cancers have been traced to the medical use of arsenic (4, 95, 178). The occupational incidence of tumors among arsenic workers has been the subject of several investigations (9, 48, 65, 101, 106, 157, 169, 178, 183). As in tobacco had little apparent effect on lung cancer incidence (59, 142). Suspensions of As in lanolin caused cancers in rats (108).

Asbestos. Lung cancer has long been associated with asbestosis in workers handling this material (14, 16, 22, 33, 46, 107, 112, 159, 180, 195). Ollivier, et al. (156), reported on skin granuloma in one patient. Inhaling long asbestos fibers induced lung fibrosis in laboratory animals (188), while injections of asbestos suspensions in lanolin induced tumors in rats (108).

Silicon. The relation of silicosis to lung cancer has been the subject of several investigations (107, 165). Implants of sand caused cancers (49, 50, 31, 32). Bentonite, a cation exchange silicate, induced tumors in mice when added to the diet (192, 193). Glass powder failed to produce tumors (45, 49, 50).

Nickel. Ni is another metal with a history of occupational lung cancer (9, 107, 131, 176, 183). Parenterally introduced Ni resulted in neoplasms in rats (102, 104), and rabbits (110), and rats placed in a chamber with nickel carbonyl developed pulmonary and liver cancers (118).

Iron. Lung cancers have been reported from workers in dusty occupations like boiler scaling (51) and iron ore mining (16). Fe_2O_3 powder was not carcinogenic to mice (152).

Gold, Silver, Platinum. All three metals produced tumors when implanted in mice (155). Gold salts, used clinically in arthritis, caused liver injury (3). Silver foil produced 32% incidence of fibrosarcoma in rats (158).

Cobalt, Zinc. Both metals induced liposarcoma in rabbits (182), and both are listed as causing occupational risks (183). Co powder produced tumors in rats (97), and $CoCl_2$ injections caused poly-

cythemia (100). Zinc salts resulted in cancers in the testes of dogs (162) and chickens (29).

Lead, Tantalum, Strontium, Selenium. Lead phosphate caused kidney adenomas in rats (199). Sarcomas were developed in rats with Ta (158), and rats fed Se for 16 months showed no tumors (120). $SrSO_4$ alone, or with benzpyrene induced neoplasms in the inguinal region (30).

Foreign Bodies. Shrapnel fragments produced lung cancer and cancer of the face after being long imbedded in veterans (161, 173). Metal tags induced neoplasms in the ears of rabbits (145).

Iodine. Chronic iodine deficiency resulted in thyroid adenomata in rats (11).

Graphite. Gloyne, et al. (73), reported two fatal cases in workers long exposed to graphite dust.

Talcum Powder. Talcum glove powder caused large granulomas 10 years after implantation in an operation (89).

Ammonium Chloride. Nemeth, et al. (154), studied the precancerous changes in the stomach of rats induced by NH_4Cl.

Hot Water. Repeated subcutaneous injection of water at 72° C. resulted in hepatic tumors in rats (189).

Acknowledgments. The original literature was made available by the Armed Forces Medical Library, and the libraries of Furman University and the Greenville General Hospital.

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SELECTED ABSTRACTS

The Treatment of Soft Tissue Infections With Tetracycline Phosphate Complex. Prigot, A., Shidlovsky, B. A. and Felix, A. J. *Antibiot. Med. & Clin. Ther. 4*:287 (1957). A new phosphate complex salt of tetracycline has been prepared and found to be more rapidly and efficiently absorbed than the hydrochloride. This salt is a stable, yellow, crystalline solid, relatively insoluble in water. It has an *in vitro* antibacterial spectrum similar to that of the hydrochloride.

In the study reported here, 500 mg. of the complex were administered orally twice a day to 103 patients with soft tissue infections. Surgical procedures were also performed where necessary. The duration of treatment ranged from 8 to 70 days, the average being 12 days.

In general the patients responded rapidly to therapy. The signs and symptoms of inflammation began to recede in 36 to 48 hours. In complicated conditions, the response was slower but satisfactory. Where surgical intervention was necessary, the incidence and magnitude of the procedures were lessened. There was also a marked decrease in morbidity and duration of hospitalization. In those infections complicating other pathologic conditions such as diabetic and arteriosclerotic gangrene, the antibiotic therapy cleared the infection so that definitive operations could be performed more quickly and with a greater degree of safety.

No toxic reactions were observed. The only side effects were noted in 3 patients who developed mild gastrointestinal symptoms, but these did not necessitate the withdrawal of the drug.

The minimal inhibitory concentrations of tetracycline phosphate complex were similar to those obtained with the hydrochloride. An appreciable blood level appeared one hour after ingestion and reached a maximum in about two hours. Higher serum levels, particularly during the first few hours after administration, were obtained with the phosphate complex than had been obtained with the hydrochloride salt of tetracycline. The clinical significance of these higher blood levels has not been determined.

Studies of Staphylococcic Resistance to Newer Antibiotics. Rantz, L. A., Randall, E., Thum, L., and Barker, L. F. *Antibiot. & Chemother. 7*:399 (1957). The three new antibiotics, vancomycin, oleandomycin, and novobiocin, have been suggested for the treatment of staphyloccic infections in man. The authors undertook a comparative *in vitro* study of these antibiotics against 41 strains of *Staphylococcus aureus* recently isolated from clinical sources.

Vancomycin was found to inhibit and kill staphylococci in low concentrations. Resistance did not develop either by the single step method or by the multiple transfer technique. However, the large molecular size of this antibiotic may make diffusion into infected tisues difficult. This was suggested by the fact that the minimal inhibitory concentration on the surface of agar plates was several times greater than in liquid media.

Eighty per cent of the strains were killed by 1 mcg. or less of novobiocin per ml. The other 20 per cent were more resistant but not out of range of concentrations that could be expected to be attained under clinical conditions. However, resistance developed with great ease. Resistant variants then required from 25 to 100 mcg. per ml. for inhibition. An example was given of a 40 fold increase in resistance to novobiocin by *S. aureus* in a clinical case, thus confirming the *in vitro* findings.

Two of nine strains of the organism resistant to both novobiocin and penicillin showed a potentiated or synergistic bactericidal effect to a combination of the two antibiotics. However, the authors warned that *in vitro* findings do not necessarily transfer to clinical situations.

The effectiveness and usefulness of oleandomycin has not yet been determined. Cross resistance between oleandomycin and erythromycin was demonstrated frequently, but not invariably, among naturally occurring organisms. Resistance to both of these antibiotics was readily produced *in vitro,* and these strains showed complete cross resistance. Potentiation of oleandomycin effectiveness by penicillin was observed in a few instances. However, resistance to oleandomycin occurred readily when penicillin resistant, oleandomycin sensitive organisms were exposed to a mixture of them. Tetracycline showed no potentiation of activity nor retardation of resistance development when combined with oleandomycin.

Each of the newer antibiotics studied has properties suggesting its value in the treatment of infection by *S. aureus,* yet each also has inherent and serious limitations.

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